Dupilumab is efficacious in patients with prurigo nodularis regardless of baseline lesion severity: pooled results from two phase 3 trials (LIBERTY-PN PRIME and PRIME2)

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Introduction: Prurigo nodularis (PN), a chronic inflammatory and pruritic skin condition with severely itchy skin nodules, substantially affects quality of life. Patients with PN are affected by highly pruritic lesions that can feature other sensations, such as stinging, burning, tingling, heat, and cold. These lesions can range in severity from a few nodules to several hundred, and in sizes from 10 millimeters to 2–3 cm.

Objective: To report the effect of dupilumab on pruritus and skin lesions in patients with PN according to the severity of their lesions at baseline, in a post hoc analysis of pooled data from two phase 3 trials.

Materials & Methods: In the two randomized, double-blind, placebo-controlled, 24-week studies LIBERTY-PN PRIME (NCT04183335) and PRIME2 (NCT04202679), adults with PN inadequately controlled by topical prescription therapies, or for whom those therapies are inadvisable, were randomized 1:1 to dupilumab 300 mg every 2 weeks or matched placebo. Efficacy was assessed from baseline to Week 24 through the Worst Itch Numerical Rating Scale
(WI-NRS; scored 0–10; high scores represent a poorer outcome), and the Investigator’s Global Assessment for PN-Stage score (IGA PN-S; scored 0–4; high scores represent more severe nodular disease). The PRIME and PRIME2 studies enrolled only patients with an IGA PN-S of 3 (moderate; 20–100 nodules) or 4 (severe; >100 nodules) at baseline.

**Results:** 311 patients were randomized (dupilumab/placebo n = 153/158), including 205 patients with moderate PN (IGA PN-S = 3) at baseline (dupilumab/placebo N = 103/102) and 104 patients with severe PN (IGA PN-S = 4) at baseline (dupilumab/placebo N = 50/54). Baseline demographics and disease characteristics were well balanced in both subgroups. At Week 24, significantly more dupilumab-treated patients achieved an IGA PN-S of 0 (no nodules) or 1 (almost clear; 1–5 nodules), whether they had moderate (52.4% vs 24.5%; nominal P = 0.0008) or severe (40.0% vs 7.4%; nominal P = 0.0014) PN at baseline, with a similar treatment effect (TE) vs placebo in both the moderate (27.9%) and severe (32.6%) subgroups. The proportion of patients with ≥3-point and ≥4-point improvement in WI-NRS, was also significantly greater in the dupilumab group than in the placebo group, whether their PN was moderate (68.9%/62.1% vs 34.3%/22.6%; nominal P = 0.0002/P < 0.0001, respectively) or severe (72.0%/66.0% vs 31.5%/25.9%; nominal P = 0.0064/P = 0.0046, resp.) at baseline. Treatment-emergent adverse events (TEAEs) occurred with higher rates in dupilumab-treated patients with moderate PN at baseline (71.6%) compared with placebo (57.8%). Patients with severe PN at baseline had similar rates of TEAEs in the dupilumab (48.0%) and placebo (55.6%) groups. Nevertheless, dupilumab-treated patients with moderate PN at baseline, and those with severe PN at baseline, had overall similar or lower rates vs placebo of serious TEAEs (3.9%/6.0% vs 8.8%/5.6%, resp.), severe TEAEs (4.9%/0.0% vs 5.9%/5.6%, resp.), and frequent TEAEs such as headache (6.9%/2.0% vs 5.9%/5.6%, resp.) and neurodermatitis (2.9%/2.0% vs 2.9%/14.8%, resp.). The incidence of conjunctivitis in dupilumab-treated patients was consistent with the
known safety profile vs placebo in both the moderate and severe groups (4.9%/2.0% vs 2.0%/0.0%, resp.).

**Conclusion:** Dupilumab treatment for 24 weeks improves itch and skin lesions in patients with PN regardless of lesion severity at baseline, with an acceptable safety profile.

**Keywords:** Prurigo nodularis, adults, therapy, baseline severity.

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